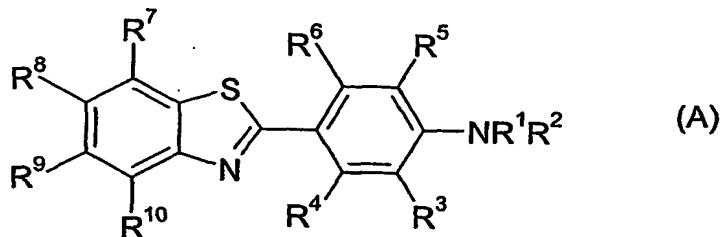


Claims

1. A process for the production of an ^{18}F -labelled tracer which comprises treatment of a solid support-bound precursor of formula (I)

5 SOLID SUPPORT-LINKER-X-TRACER (I)

wherein X is a group which promotes nucleophilic substitution at a specific site on the attached TRACER and the TRACER is of formula (A)



10

wherein:

R^1 and R^2 are independently selected from hydrogen, a protecting group, C_{1-6} alkyl, C_{1-6} hydroxyalkyl, and C_{1-6} haloalkyl;

15 R^3 to R^{10} are independently selected from hydrogen, halo, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} hydroxyalkyl, C_{1-6} alkoxy, C_{1-6} haloalkoxy, hydroxy, cyano, and nitro; and one of the groups R^1 to R^{10} is bonded to the SOLID SUPPORT-LINKER-X-;

with $^{18}\text{F}^-$ to produce the labelled tracer of formula (II)

20 ^{18}F -TRACER (II)

wherein the TRACER is as defined for the compound of formula (I) except that one of the groups R^1 to R^{10} is bonded to the ^{18}F instead of to the SOLID SUPPORT-LINKER-X – in formula (I);

optionally followed by:

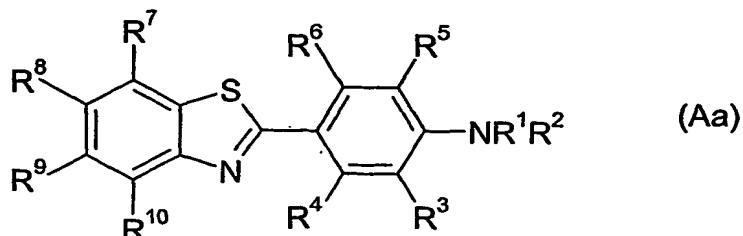
25 (i) removal of excess $^{18}\text{F}^-$, for example by ion-exchange chromatography; and/or
 (ii) removal of any protecting groups; and/or
 (iii) removal of organic solvent; and/or
 (iv) formulation of the resultant compound of formula (II) as an aqueous solution

2. A process according to claim 1 which comprises treatment of a solid support-bound precursor of formula (Ia):

SOLID SUPPORT-LINKER-SO₂-O -TRACER (Ia)

5

wherein the TRACER is of formula (Aa)



wherein:

10 R¹ and R² are independently selected from hydrogen, a protecting group, C₁₋₆ alkyl, C₁₋₆ hydroxyalkyl, and C₁₋₆ haloalkyl;
 R³ to R¹⁰ are independently selected from hydrogen, halo, C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₁₋₆ hydroxyalkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkoxy, hydroxy, cyano, and nitro;
in which either (a) an R¹ C₁₋₆ alkyl group or (b) an R³ to R¹⁰ C₁₋₆ alkyl or C₁₋₆ alkoxy group is bonded to the SOLID SUPPORT-LINKER-SO₂-O – in formula (Ia);

15

with ¹⁸F⁻ to produce the labelled tracer of formula (IIa)

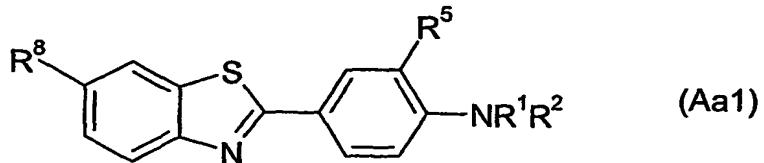
¹⁸F-TRACER (IIa)

20 wherein the TRACER is as defined for the compound of formula (Ia) except that either (a) an R¹ C₁₋₆ alkyl group or (b) an R³ to R¹⁰ C₁₋₆ alkyl or C₁₋₆ alkoxy group is bonded to the ¹⁸F instead of to the SOLID SUPPORT-LINKER-SO₂-O – in formula (Ia);

optionally followed by:

25 (i) removal of excess ¹⁸F⁻, for example by ion-exchange chromatography; and/or
 (ii) removal of any protecting groups; and/or
 (iii) removal of organic solvent; and/or
 (iv) formulation of the resultant compound of formula (IIa) as an aqueous solution.

3. A process according to claim 2 wherein the TRACER is of formula (Aa1)



5 wherein

R^1 and R^2 are independently selected from hydrogen, a protecting group, C_{1-6} alkyl, C_{1-6} hydroxyalkyl, and C_{1-6} haloalkyl;

R^5 is hydrogen or C_{1-6} alkyl,

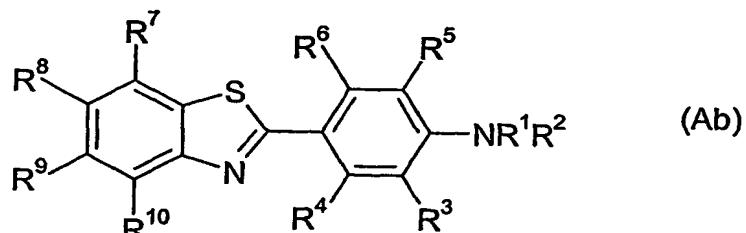
10 R^8 is hydroxy, C_{1-6} alkoxy, C_{1-6} haloalkyl, or C_{1-6} alkyl;

provided that one of R^1 , R^5 and R^8 is C_{1-6} alkyl bonded to the SOLID SUPPORT-LINKER- SO_2-O – in formula (la) or R^8 is C_{1-6} alkoxy bonded to the SOLID SUPPORT-LINKER- SO_2-O – in formula (la) .

15 4. A process according to claim 1 which comprises treatment of a solid support-bound precursor of formula (lb)



wherein Y^- is an anion and the TRACER is of formula (Ab)



20

wherein:

R^1 and R^2 are independently selected from hydrogen, a protecting group, C_{1-6} alkyl, C_{1-6} hydroxyalkyl, and C_{1-6} haloalkyl;

25

one of R^3 to R^{10} is a bond to the SOLID SUPPORT-LINKER- I^- group in formula (lb) and the others are independently selected from hydrogen, halo, C_{1-6} alkyl, C_{1-6}

haloalkyl, C₁₋₆ hydroxyalkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkoxy, hydroxy, cyano, and nitro;

with ¹⁸F⁻ to produce the labelled tracer of formula (IIb)

5

¹⁸F-TRACER (IIb)

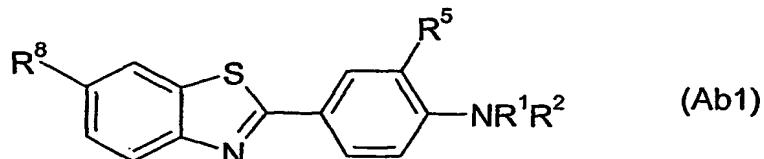
wherein the TRACER is as defined for the compound of formula (Ib) except that one of R³ to R¹⁰ is a bond to the ¹⁸F instead of a bond to the SOLID SUPPORT-LINKER-I⁺- group in formula (Ib);

10 optionally followed by:

- (i) removal of excess ¹⁸F⁻, for example by ion-exchange chromatography; and/or
- (ii) removal of any protecting groups; and/or
- (iii) removal of organic solvent; and/or
- (iv) formulation of the resultant compound of formula (IIb) as an aqueous solution.

15

5. A process according to claim 4 wherein the TRACER is a compound of formula (Ab1)



wherein:

20

R¹ and R² are independently selected from hydrogen, a protecting group, C₁₋₆ alkyl, C₁₋₆ hydroxyalkyl, and C₁₋₆ haloalkyl;

R⁵ is hydrogen, C₁₋₆ alkyl, or a bond to the SOLID SUPPORT-LINKER-I⁺- group in formula (Ib);

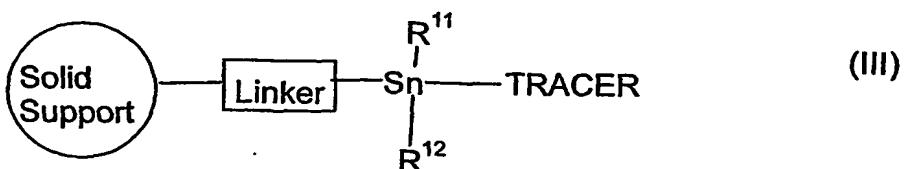
25

R⁸ is hydroxy, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ alkyl, or a bond to the SOLID SUPPORT-LINKER-I⁺- group in formula (Ib);

provided that only one of R⁵ and R⁸ is a bond to the SOLID SUPPORT-LINKER-I⁺- group in formula (Ib).

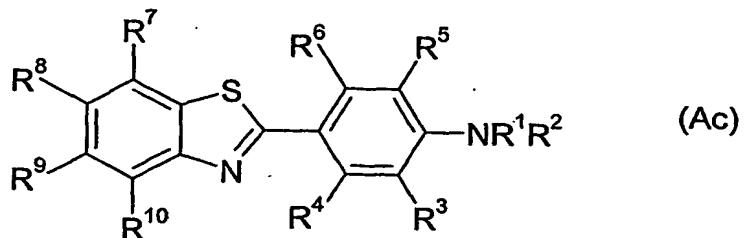
30 6. A process for the production of an ¹⁸F-labelled tracer which comprises

treatment of a solid support-bound precursor of formula (III):



wherein R¹¹ and R¹² are independently selected from C₁₋₆ alkyl and the TRACER

5 is a compound of formula (Ac):



wherein:

R¹ and R² are independently selected from hydrogen, a protecting group,

10 C₁₋₆ alkyl, C₁₋₆ hydroxyalkyl, and C₁₋₆ haloalkyl;

one of R³ to R¹⁰ is a bond to the Sn in formula (III) and the others are independently selected from hydrogen, halo, C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₁₋₆ hydroxyalkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkoxy, hydroxy, cyano, and nitro;

15

with a source of ¹⁸F, suitably ¹⁸F₂, ¹⁸F-CH₃COOF or ¹⁸F-OF₂;

to give the labelled tracer of formula (IV);

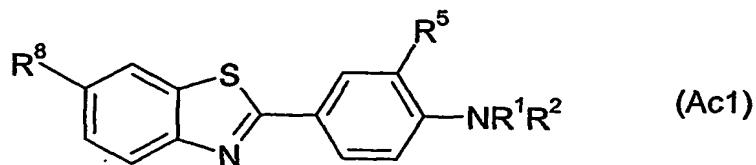
20 ¹⁸F-TRACER (IV)

wherein the TRACER is as defined for the compound of formula (III) except that one of R³ to R¹⁰ is a bond to the ¹⁸F instead of a bond to the Sn in formula (III); optionally followed by:

- (i) removal of excess fluorinating agent and ¹⁸F⁻ ions produced in the generation 25 of the fluorinating agent or in the reaction; and/or
- (ii) removal of any protecting groups; and/or

- (iii) removal of organic solvent; and/or
- (iv) formulation of the resultant compound of formula (IV) as an aqueous solution.

7. A process according to claim 6 in which the TRACER is suitably a compound of
5 formula (Ac1)



wherein:

10 R¹ and R² are independently selected from hydrogen, a protecting group, C₁₋₆ alkyl, C₁₋₆ hydroxyalkyl, and C₁₋₆ haloalkyl;

R⁵ is hydrogen, C₁₋₆ alkyl, or a bond to the Sn in formula (III);

R⁸ is hydroxy, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ alkyt, or a bond to the Sn in formula (III);

provided that only one of R⁵ and R⁸ is a bond to the Sn in formula (III).

15

8. A process for the preparation of a ¹⁸F-labelled tracer of formula (II), (IIa), (IIb), or (IV), according to any one of claims 1 to 7, for use in PET.

9. A compound of formula (I), (Ia), (Ib), (III) as defined in any one of claims 1 to 7.

20

10. A radiopharmaceutical kit for the preparation of an ¹⁸F-labelled tracer for use in PET, which comprises:

(i) a vessel containing a compound of formula (I), (Ia), or (Ib) as defined in any one of claims 1 to 5; and

25 (ii) means for eluting the vessel with a source of ¹⁸F⁻;

(iii) an ion-exchange cartridge for removal of excess ¹⁸F⁻; and optionally

(iv) a cartridge for solid-phase deprotection of the resultant product of formula (II), (IIa), or (IIb) as defined in any one of claims 1 to 5.

30 11. A cartridge for a radiopharmaceutical kit for the preparation of an ¹⁸F-labelled

tracer for use in PET which comprises:

- (i) a vessel containing a compound of formula (I), (Ia), or (Ib) as defined in any one of claims 1 to 5; and
- (ii) means for eluting the vessel with a source of $^{18}\text{F}^-$.

5

12. A radiopharmaceutical kit for the preparation of an ^{18}F -labelled tracer for use in PET, which comprises:

- (i) a vessel containing a compound of formula (III) as defined in claim 6 or 7; and
- (ii) means for eluting the vessel with a source of $^{18}\text{F}^-$; and optionally
- (iii) a cartridge for removal of excess fluorinating agent and $^{18}\text{F}^-$ ions; and optionally
- (iv) a cartridge for solid-phase deprotection of the resultant product of formula (IV) as defined in claim 6 or 7.

10

13. A cartridge for a radiopharmaceutical kit for the preparation of an ^{18}F -labelled tracer according to claim 12 for use in PET which comprises:

- (i) a vessel containing a compound of formula (III) as defined in claim 6 or 7; and
- (ii) means for eluting the vessel with a source of $^{18}\text{F}^-$.

15

14. A method for obtaining a diagnostic PET image which comprises the step of using a radiopharmaceutical kit according to claim 10 or 12 or a cartridge for a radiopharmaceutical kit according to claim 11 or 13.